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TITLE: Coated implantable medical device

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Abstract Text - ABTX (1):

A coated implantable medical device 10 includes a structure 12 adapted for introduction into the vascular system, esophagus, trachea, colon, biliary tract, or urinary tract; at least one coating layer 16 posited on one surface of the structure; and at least one layer 18 of a bioactive material posited on at least a portion of the coating layer 16, wherein the coating layer 16 provides for the controlled release of the bioactive material from the coating layer. In addition, at least one porous layer 20 can be posited over the bioactive material layer 18, wherein the porous layer is includes a **polymer** and provides for the controlled release of the bioactive material therethrough. Preferably, the structure 12 is a coronary stent. The porous layer 20 includes a **polymer** applied preferably by vapor or plasma deposition and provides for a controlled release of the bioactive material. It is particularly preferred that the **polymer** is a polyamide, parylene or a parylene derivative, which is deposited without solvents, heat or catalysts, and merely by condensation of a monomer vapor.

Brief Summary Text - BSTX (13):

The foregoing problems are solved and a technical advance is achieved in an illustrative vascular stent or other implantable medical

device that provides a controlled release of an agent, drug or bioactive material into the vascular or other system, or other location in the body, in which a stent or other device is positioned. Applicants have discovered that the degradation of the agent, a drug or a bioactive material that is applied to such a device can be avoided by positing a coating layer on one surface of the device structure. The agent, drug or bioactive material is posited over at least a portion of the coating layer, wherein the coating layer provides for a controlled release of the bioactive material posited thereon. Furthermore, the medical device further includes a porous layer posited over the bioactive material wherein the porous layer is composed of a **polymer and the polymer** provides for a controlled release of the bioactive material through the porous layer.

Brief Summary Text - BSTX (17):

Applicants have also discovered that the degradation of an agent, a drug or a bioactive material applied to such a device may be avoided by covering the agent, drug or bioactive material with a porous layer of a biocompatible **polymer** that is applied without the use of solvents, catalysts, heat or other chemicals or techniques, which would otherwise be likely to degrade or damage the agent, drug or material. Those biocompatible **polymers** may be applied preferably by vapor deposition or plasma deposition, and may polymerize and cure merely upon condensation from the vapor phase, or may be photolytically polymerizable and are expected to be useful for this purpose. However, it should be recognized that other coating techniques may also be employed.

Brief Summary Text - BSTX (19):

The at least one porous layer is preferably composed of a polyamide, parylene or a parylene derivative applied by catalyst-free vapor deposition and is conveniently about 5,000 to 250,000 .ANG. thick, which is adequate to provide a controlled release of the bioactive material. "Parylene" is both a generic name for a known group of **polymers** based on p-xylylene and made by vapor phase polymerization, and a name for the unsubstituted form of the **polymer**; the latter usage is employed herein. More particularly, parylene or a parylene derivative is created by first heating p-xylene or a suitable derivative at an appropriate temperature (for example, at about 950.degree. C.) to produce the cyclic dimer di-p-xylylene (or a derivative thereof). The resultant solid can be separated in pure form, and then cracked and pyrolyzed at an appropriate temperature (for example, at about 680.degree. C.) to produce a monomer vapor of p-xylylene (or derivative); the monomer vapor is cooled to a suitable temperature (for example, below 50.degree. C.) and allowed to condense on the desired object, for example, on the at least one layer of bioactive material. The resultant **polymer** has the repeating structure .paren open-st.CH.sub.2 C.sub.6 H.sub.4 CH.sub.2.paren close-st..sub.n, with n equal to about 5,000, and a molecular weight in the range of 500,000.

Brief Summary Text - BSTX (21):

The at least one porous layer can alternatively be applied by plasma deposition. Plasma is an ionized gas maintained under vacuum and excited by electrical energy, typically in the radiofrequency range. Because the gas is maintained under vacuum, the plasma deposition process occurs at or near room temperature. Plasma can be used to deposit **polymers** such

as poly(ethylene oxide), poly(ethylene glycol), and poly(propylene oxide), as well as **polymers** of silicone, methane, tetrafluoroethylene (including TEFLON brand **polymers**), tetramethyldisiloxane, and others.

Brief Summary Text - BSTX (22):
While the foregoing represents some preferred embodiments of the present invention, other **polymer** systems may also be employed, e.g., **polymers** derived from photopolymerizeable monomers. Also, other coating techniques may be utilized, e.g., dipping, spraying, and the like.

Brief Summary Text - BSTX (23):
The device may include two or more layers of different bioactive materials atop the structure. However, for the purposes of the present invention, the same bioactive material will generally not be posited on the different surfaces of the device within the same layer. In other words, each surface of the device structure will carry a different bioactive material or materials except where the bioactive material is the innermost or outermost layer, e.g. heparin may form the innermost layer or the outermost layer or both. These additional layers may be placed directly atop one another or can be separated by additional porous **polymer** layers between each of them. Additionally, the layers of bioactive materials can comprise a mixture of different bioactive materials. The porous layers are also preferably composed of parylene or a parylene derivative. Advantageously, the two or more bioactive materials can have different solubilities, and the layer containing the less soluble bioactive material (for example, dexamethasone) is preferably posited above the layer containing the more soluble bioactive material (for

example, heparin).
Unexpectedly, this has been found to increase the in vitro release rate of some relatively less soluble materials such as dexamethasone, while simultaneously decreasing the release rate of some relatively more soluble materials such as heparin.

Brief Summary Text - BSTX (24):
While the structure included in the device may be configured in a variety of ways, the structure is preferably configured as a vascular **stent** composed of a biocompatible metal such as stainless steel, nickel, silver, platinum, gold, titanium, tantalum, iridium, tungsten, Nitinol, inconel, or the like. An additional substantially nonporous **coating** layer of parylene or a parylene derivative or other biocompatible **polymer** of about 50,000 to 500,000 .ANG. **thick** may be posited directly atop the vascular **stent,** beneath the at least one layer of bioactive material. The additional **coating** layer can merely be relatively less porous than the at least one porous layer, but preferably is substantially nonporous, that is, sufficiently nonporous to render the **stent** essentially impervious to blood during normal circumstances of use.

Brief Summary Text - BSTX (25):
The device and methods of the present invention are useful in a wide variety of locations within a human or veterinary patient, such as in the esophagus, trachea, colon, biliary tract, urinary tract and vascular system, as well as for subdural and orthopedic devices, implants or replacements. They are particularly advantageous for reliably delivering suitable bioactive materials during or following an intravascular procedure, and find particular use in

preventing abrupt closure and/or restenosis of a blood vessel. More particularly, they permit, for example, the delivery of an antithrombotic, an antiplatelet, an anti-inflammatory steroid, or another medication to the region of a blood vessel which has been opened by PTA. Likewise, it allows for the delivery of one bioactive material to, for example, the lumen of a blood vessel and another bioactive material to the vessel wall. The use of a porous **polymer** layer permits the release rate of a bioactive material to be carefully controlled over both the short and long terms.

Drawing Description Text - DRTX (13):
FIG. 11 depicts another aspect of the medical device of FIG. 1 utilizing a **polymer** coating layer with a bioactive material attached thereto; and

Drawing Description Text - DRTX (14):
FIG. 12 depicts still another aspect of the medical device of FIG. 11 in which the **polymer** coating layer is adhered to the outer surface of the device base material using an adhesive promotion layer.

Detailed Description Text - DETX (7):
A variety of conventional materials can be employed as the base material 14. Some materials may be more useful for structures other than the coronary stent exemplifying the structure 12. The base material 14 may be either elastic or inelastic, depending upon the flexibility or elasticity of the **polymer** layers to be applied over it. The base material may be either biodegradable or non-biodegradable, and a variety of biodegradable **polymers** are known. Moreover, some biologic agents have sufficient strength to serve as the base material 14 of some useful structures 12, even if not

especially useful in the
exemplary coronary stent.

Detailed Description Text - DETX (8):

Accordingly, the base material 14 can include at least one of stainless steel, tantalum, titanium, nitinol, gold, platinum, inconel, iridium, silver, tungsten, or another biocompatible metal, or alloys of any of these; carbon or carbon fiber; cellulose acetate, cellulose nitrate, silicone, polyethylene teraphthalate, polyurethane, polyamide, polyester, polyorthoester, polyanhydride, polyether sulfone, polycarbonate, polypropylene, high molecular weight polyethylene, polytetrafluoroethylene, or another biocompatible polymeric material, or mixtures or copolymers of these; polylactic acid, polyglycolic acid or copolymers thereof, a polyanhydride, polycaprolactone, polyhydroxybutyrate valerate or another biodegradable **polymer,** or mixtures or copolymers of these; a protein, an extracellular matrix component, collagen, fibrin or another biologic agent; or a suitable mixture of any of these. Stainless steel is particularly useful as the base material 14 when the structure 12 is configured as a vascular stent.

Detailed Description Text - DETX (21):

More particularly, the porous layer 20 is composed of a **polymer** deposited on the bioactive material layer 18, preferably by vapor deposition. Plasma deposition may also be useful for this purpose. Preferably, the layer 20 is one that is polymerized from a vapor which is free of any solvent, catalysts or similar polymerization promoters. Also preferably, the **polymer** in the porous layer 20 is one which automatically polymerizes upon condensation from the vapor phase, without the action of any curative agent or

activity such as heating, the application of visible or ultraviolet light, radiation, ultrasound, or the like. Most preferably, the **polymer** in the porous layer 20 is polyimide, parylene or a parylene derivative.

Detailed Description Text - DETX (23):

As shown in FIG. 1, the device 10 of the present invention can further comprise at least one additional coating layer 16 posited between the structure 12 and the at least one layer 18 of bioactive material. While the additional coating layer 16 can simply be a medical grade primer, the additional coating layer 16 is preferably composed of the same **polymer** as the at least one porous layer 20. However, the additional coating layer 16 is also preferably less porous than the at least one porous layer 20, and is more preferably substantially nonporous. "Substantially nonporous" means that the additional coating layer 16 is sufficiently impervious to prevent any appreciable interaction between the base material 14 of the structure 12 and the blood to which the device 10 will be exposed during use. The use of an additional coating layer 16 which is substantially nonporous would permit the use of a toxic or poisonous base material 14, as mentioned above. Even if the base material 14 of the structure 12 is biocompatible, however, it may be advantageous to isolate it from the blood by use of a substantially nonporous coating layer 16.

Detailed Description Text - DETX (24):

Other **polymer** systems that may find application within the scope of the invention include **polymers** derived from photopolymerizable monomers such as liquid monomers preferably having at least two cross

linkable C--C (Carbon to
Carbon) double bonds and being a non-gaseous addition polymerizable
ethylenically unsaturated compound, having a boiling point above 100.degree.
C., at atmospheric pressure, a molecular weight of about 100-1500 and being
capable of forming high molecular weight addition **polymers** readily. More
preferably, the monomer is preferably an addition photopolymerizable
polyethylenically unsaturated acrylic or methacrylic acid ester containing two
or more acrylate or methacrylate groups per molecule or mixtures thereof. A
few illustrative examples of such multifunctional acrylates are ethylene glycol
diacrylate, ethylene glycol dimethacrylate, trimethylopropane triacrylate,
trimethylopropane trimethacrylate, pentaerythritol tetraacrylate or
pentaerythritol tetramethacrylate, 1,6-hexanediol dimethacrylate, and
diethyleneglycol dimethacrylate.

Detailed Description Text - DETX (26):

Other useful **polymer** systems include a **polymer** that is biocompatible and
minimizes irritation to the vessel wall when the stent is implanted. The
polymer may be either a biostable or a bioabsorbable **polymer** depending on the
desired rate of release or the desired degree of **polymer** stability, but a
bioabsorbable **polymer** is preferred for this embodiment since, unlike a
biostable **polymer,** it will not be present long after implantation to cause any
adverse, chronic local response. Bioabsorbable **polymers** that could be used
include poly(L-lactic acid), polycaprolactone, poly(lactide-co-glycolide),
poly(hydroxybutyrate), poly(hydroxybutyrate-co-valerate), polydioxanone,
polyorthoester, polyanhydride, poly(glycolic acid), poly(D,L-lactic acid),
poly(glycolic acid-co-trimethylene carbonate),

polyphosphoester,
polyphosphoester urethane, poly(amino acids),
cyanoacrylates, poly(trimethylene
carbonate), poly(iminocarbonate), copoly(ether-esters)
(e.g., PEO/PLA),
polyalkylene oxalates, polyphosphazenes and biomolecules
such as fibrin,
fibrinogen, cellulose, starch, collagen and hyaluronic
acid. Also, biostable
polymers with a relatively low chronic tissue response such
as polyurethanes,
silicones, and polyesters could be used and other **polymers**
could also be used
if they can be dissolved and cured or polymerized on the
stent such as
polyolefins, polyisobutylene and ethylene-alphaolefin
copolymers; acrylic
polymers and copolymers, vinyl halide **polymers** and
copolymers, such as
polyvinyl chloride; polyvinyl ethers, such as polyvinyl
methyl ether;
polyvinylidene halides, such as polyvinylidene fluoride and
polyvinylidene
chloride; polyacrylonitrile, polyvinyl ketones; polyvinyl
aromatics, such as
polystyrene, polyvinyl esters, such as polyvinyl acetate;
copolymers of vinyl
monomers with each other and olefins, such as
ethylene-methyl methacrylate
copolymers, acrylonitrile-styrene copolymers, ABS resins,
and ethylene-vinyl
acetate copolymers; polyamides, such as Nylon 66 and
polycaprolactam; alkyd
resins, polycarbonates; polyoxymethylenes; polyimides;
polyethers; epoxy
resins, polyurethanes; rayon; rayon-triacetate; cellulose,
cellulose acetate,
cellulose butyrate; cellulose acetate butyrate; cellophane;
cellulose nitrate;
cellulose propionate; cellulose ethers; and carboxymethyl
cellulose.

Detailed Description Text - DETX (27):
While plasma deposition and vapor phase deposition may
be a preferred method
for applying the various coatings on the stent surfaces,
other techniques may

be employed. For example, a **polymer** solution may be applied to the stent and the solvent allowed to evaporate, thereby leaving on the stent surface a coating of the **polymer** and the therapeutic substance. Typically, the solution can be applied to the stent by either spraying the solution onto the stent or immersing the stent in the solution. Whether one chooses application by immersion or application by spraying depends principally on the viscosity and surface tension of the solution, however, it has been found that spraying in a fine spray such as that available from an airbrush will provide a coating with the greatest uniformity and will provide the greatest control over the amount of coating material to be applied to the stent. In either a coating applied by spraying or by immersion, multiple application steps are generally desirable to provide improved coating uniformity and improved control over the amount of therapeutic substance to be applied to the stent.

Detailed Description Text - DETX (31):
In still another aspect of the present invention as depicted in FIG. 11, **coating** layer 16 can be considered an adsorbent layer and/or an absorbent layer in which a bioactive material is attached thereto. In one particular example, device 10 is a stainless steel GR II.TM. **stent** in which the stainless steel base material 14 of structure 12 is **coated with a polymer** and, in particular, parylene. This adsorbent **polymer** layer 16 of parylene is approximately 230,000 .ANG. **thick**. Bioactive material layer 18 of the antiplatelet GP IIb/IIIa antibody (AZ1) was passively loaded on adsorbent **polymer** layer 16. The **polymer** **coated** stainless steel **stents** were immersed for approximately 24 hours in a buffered aqueous solution of AZ1 antibody (1 mg/ml, pH=7.2) at 37.degree. C.

AZ1 is a monoclonal anti-rabbit platelet glycoprotein (GP) IIb/IIIa antibody. Using radio-labeled AZ1, it was demonstrated that approximately 0.02 .mu.g antibody was loaded per mm.sup.2 **stent** surface area (approximately 2 .mu.g total for a 3.times.20 mm GR II.TM. **stent**). it was also demonstrated that in an in-vitro flow system (10 ml/min, 1% BSA in PBS) approximately half the loaded antibody remained on the **stent** after approximately 10 days perfusion.

Detailed Description Text - DETX (32):
The mechanism by which the stent is loaded with drug are thought to include adsorption onto the surface of the **polymer** layer and/or absorption into the **polymer**.

Detailed Description Text - DETX (33):
Previous studies with similar loading and release of AZ1 from cellulose coated stainless steel stents showed inhibition of platelet aggregation and reduced thrombosis rates in a rabbit model of deep arterial injury. (Aggarwal et al., Antithrombotic Potential of **Polymer**-Coated Stents Eluting Platelet Glycoprotein IIb/IIIa Receptor Antibody, American Heart Association Circulation Vol. 94 No. 12, Dec. 15, 1996, pp3311-3317).

Detailed Description Text - DETX (34):
In another example, c7E3 Fab as bioactive material layer 18 is attached to **polymer** coating layer 16. Bioactive material c7E3 Fab is a chimeric monoclonal antibody that acts upon the Gp IIa/IIIb integrin on platelets to inhibit their aggregation. This antibody or receptor blocker can be used in humans intravenously to prevent thrombosis during coronary angioplasty. This receptor blocker is also known as ReoPro.TM. available from Eli

Lilly, Indianapolis,
Ind. Bioactive material layer 18 of the antiplatelet GP IIb/IIIa antibody
(c7E3 Fab) was passively loaded on adsorbent **polymer** layer 16. The **polymer**
coated stainless steel stents were immersed for approximately 24 hours in a
buffered aqueous solution of c7E3 Fab antibody (1 mg/ml, pH=7.2) at 37.degree.
C. c7E3 Fab is an inhibitor of platelet thrombus in humans. Using
radio-labeled c7E3 Fab, it was demonstrated that approximately 0.10 .mu.g
antibody was loaded per mm.sup.2 stent surface area (approximately 10 .mu.g
total for a 3.times.20 mm GR II.TM. stent). It was also demonstrated that in
an in-vitro flow system (10 ml/min, 1% BSA in PBS) approximately half the
loaded antibody remained on the stent after approximately 10 days perfusion.
As is known, the extent of adsorption depends on the temperature as well as the
surface area of the adsorbent. There are basically two kinds of adsorption:
physical adsorption (also referred to as physisorption) and chemical adsorption
(also referred to as chemisorption). The forces in physisorption are low
between the adsorbent surface and the adsorbate molecules. The energies of
adsorption are generally less than 3 kJ mol.sup.31 1. Physisorption is usually
reversible. The binding forces in chemisorption are much stronger than in
physisorption, and the energies of adsorption range up to 400 kJ mol.sup.-1.
Chemisorption is much less reversible than physisorption. The adsorption of
c7E3 Fab on adsorbent **polymer** layer 16 is believed to be chemisorption.

Detailed Description Text - DETX (37):
More recently, paclitaxel coated stents have also been shown to reduce
neointimal hyperplasia in a porcine coronary in-stent restenosis model. It has

been shown that GR II.TM. stents coated with "slow-release" paclitaxel (175-200 .mu.g total drug with in vitro release kinetics of 0.75 .mu.g/day for the first 30 days) significantly reduced in-stent restenosis compared with controls (Table 1). Furthermore, the coating itself appears biocompatible.
The adsorption of paclitaxel on base material 14 or on adsorbent **polymer** layer 16 is believed to be physisorption.

Detailed Description Text - DETX (39):
The results of these studies suggest that paclitaxel-**coated stents** can possibly and effectively prevent restenosis by eliminating geometric remodeling and reducing neointimal hyperplasia. These findings are especially important for high-risk lesion subsets, such as aorto-ostial lesions or small vessel, and can not only improve the long-terms results of **stents** but also extend the indications for **stent** implantation. These studies were conducted with **coating** layer 16 of, for example, parylene ranging in **thickness** from preferrably 10 to 1000 k.ANG., more preferrably 20 to 250 k.ANG., and even more preferrably 230 k.ANG.. It is also submitted that concentrations of paclitaxel can be posited on base material 14 or adsorbent **polymer** layer 16. These concentrations can range from 0.6 mg/mm.sup.2 to 60 mg/mm.sup.2, preferably 1.5 mg/mm.sup.2 to 5 mg/mm.sup.2, and more preferably 1.8 mg/mm.sup.2. Paclitaxel has low solubility in water, but may be taken up by tissue proteins and lipids when in contact therewith.

Detailed Description Text - DETX (52):
FIG. 12 depicts still another aspect of device 10 of FIG. 11. In this embodiment, a parylene adhesion promotion layer 30 is first applied to

stainless steel base material 14 of structure 12. By way of example, adhesion promotion layer 30 is a thin layer of silane having a **thickness** in the range of, for example, 0.5 to 5,000 .ANG. and preferrably, 2 to 50 .ANG.. This silane promotion layer is preferrably A-174 silane including a gamma-methacryloxypropytrimethoxysilane, which is available from Specialty **Coating** Systems Inc., Indianapolis, Ind. In preparing the outer surface of base material 14, it is first cleaned with isopropyl alcohol. The **stent** is then dipped in the silane to apply a very thin layer thereof to the outer surface of the base material. **Polymer coating** layer 16 of parylene is then applied to the silane layer. Other methods of preparing the outer surface of base material 14 include plasma etching and grit blasting. Preparation includes cleaning the outer surface of the base material with isopropyl alcohol, plasma etching the outer surface of the base material and applying the silane to the plasma etched surface. With grit blasting, the outer surface of the base material is grit blasted and then cleaned with isopropyl alcohol to which silane is applied to the cleansed grit blasted surface.

Detailed Description Text - DETX (54):

The device 10 of the present invention can further comprise an additional porous layer 24 of the **polymer** posited between each of the layers 18 and 22 of bioactive material. It is reiterated that bioactive material 18 is on one surface of structure 12. The other surface may be free of bioactive material or may comprise one or more different bioactive materials. The additional porous layer 24 can give the bioactive materials in the layers 18 and 22 different release rates. Simultaneously, or alternatively,

the device 10 may employ bioactive materials in the two layers 18 and 22 which are different from one another and have different solubilities. In such a case, it is advantageous and preferred to position the layer 22 containing the less soluble bioactive material above the layer 18 containing the more soluble bioactive material. Alternatively, the bioactive material 18 may be contained in holes, wells, slots and the like occurring within the stent surface as illustrated in FIGS. 8-10 and will further be discussed in greater detail.

Detailed Description Text - DETX (56):
The bioactive material layers 18 and/or 22 are applied to the device 10 independent of the application of the porous **polymer** layers 20 and/or 24. Any mixing of a bioactive material from the layers 18 and/or 22 into the porous layers 20 and/or 24, prior to introducing the device 10 into the vascular system of the patient, is unintentional and merely incidental. This gives significantly more control over the release rate of the bioactive material than the simple dispersal of a bioactive material in a polymeric layer.

Detailed Description Text - DETX (64):
Any of the porous **polymer** layers 20 and 24 may also be surface processed by any of the methods mentioned above to alter the release rate of the bioactive material or materials, and/or otherwise improve the biocompatibility of the surface of the layers. For example, the application of an overcoat of polyethylene oxide, phosphatidylcholine or a covalently bound bioactive material, e.g., covalently attached heparin to the layers 20 and/or 24 could render the surface of the layers more blood compatible. Similarly, the plasma

treatment or application of a hydrogel coating to the layers 20 and/or 24 could alter their surface energies, preferably providing surface energies in the range of 20 to 30 dynes/cm.sup.2, thereby rendering their surfaces more biocompatible.

Detailed Description Text - DETX (74):

The method of making the device 10 according to the present invention may now be understood. In its simplest form, the method comprises the steps of depositing the at least one layer 18 of bioactive material over the structure 12, followed by depositing the at least one porous layer 20, preferably by vapor deposition or plasma deposition, over the at least one bioactive material layer 18 on the one surface of structure 12, the at least one porous layer 20 being composed of a biocompatible **polymer** and being of a thickness adequate to provide a controlled release of the bioactive material. Preferably, the at least one additional coating layer 16 is first posited by vapor deposition directly on the base material 14 of the structure 12. Such deposition is carried out by preparing or obtaining di-p-xylylene or a derivative thereof, sublimating and cracking the di-p-xylylene or derivative to yield monomeric p-xylylene or a monomeric derivative, and allowing the monomer to simultaneously condense on and polymerize over the base material 14. The deposition step is carried out under vacuum, and the base material 14 maintained at or near room temperature during the deposition step. The deposition is carried out in the absence of any solvent or catalyst for the **polymer,** and in the absence of any other action to aid polymerization. One preferred derivative for carrying out the deposition step is

dichloro-di-p-xylylene. The parylene or parylene derivative is preferably applied at the thickness disclosed above, to yield a coating layer 16 which is substantially nonporous, but in any event less porous than the at least one porous layer 20 to be applied. If required by the composition of the coating layer 16, the layer 16 is then surface processed in an appropriate manner, for example, by plasma treatment as disclosed above.

Detailed Description Text - DETX (80):
In any event, once the bioactive material layer 18 is in place, the at least one porous layer 20 is then applied over the at least one bioactive material layer 18 in the same manner as for the application of the at least one additional coating 16. A **polymer** such as parylene or a parylene derivative is applied at the lesser thickness disclosed above, however, so as to yield the at least one porous layer 20.

Detailed Description Text - DETX (82):
Of course, polyimide may be deposited as any or all of the porous and additional coating layers 20, 24 and/or 16 by vapor deposition in a manner similar to that disclosed above for parylene and its derivatives. Techniques for the plasma deposition of **polymers** such as poly(ethylene oxide), poly(ethylene glycol), poly(propylene oxide), silicone, or a **polymer** of methane, tetrafluoroethylene or tetramethyl-disiloxane on other objects are well-known, and these techniques may be useful in the practice of the present invention.

Detailed Description Text - DETX (84):
The method of using the device 10 of the present invention in medically

treating a human or veterinary patient can now be easily understood as well.
The method of the present invention is an improvement over previous methods which include the step of inserting into a patient an implantable vascular device 10, the device 10 comprising a structure 12 adapted for introduction into the vascular system of a patient, and the structure 12 being composed of a base material 14. The method according to the present invention comprises the preliminary steps of depositing at least one layer 18 of a bioactive material on one surface of the structure 12, followed by depositing at least one porous layer 20 over the at least one bioactive material layer 18, the porous layer 20 being composed of a **polymer** and having a thickness adequate to provide a controlled release of the bioactive material when the device 10 is positioned in the patient's vascular system.

Detailed Description Text - DETX (88):
In view of the disclosure above, it is clear that the present invention provides an implantable medical device which achieves precise control over the release of one or more bioactive materials contained in the device. Moreover, the polyimide, parylene, parylene derivative or other polymeric layers 16, 20 and/or 24 can be remarkably thin, in comparison to the thicknesses required for other **polymer** layers. The bulk or substantial majority of the overall coating on the structure 12 can therefore consist of bioactive material. This allows the supply of relatively large quantities of bioactive material to the patient, much greater than the amounts supplied by prior devices. These quantities of bioactive material can be supplied to any of a wide variety of locations within a patient during or after the performance of a medical procedure, but are

especially useful for preventing abrupt closure and/or restenosis of a blood
vessel by the delivery of an antithrombic or other medication to the region of
it which has been opened by PTA. The invention permits the release rate of a
bioactive material to be carefully controlled over both the short and long
terms. Most importantly, any degradation of the bioactive material which might
otherwise occur by other **polymer** coating techniques is avoided.

Detailed Description Paragraph Table - DETL (4):
TABLE 4 One-Month QCA Data (Mean .+-. Standard **Deviation**) Mean Diameter
Mean Diameter Late Paclitaxel Pre-procedure at Follow-up MLD at F/U Loss
(.mu.g) (mm) BAR (mm) (mm) (%) 0 2.80 .+-. 0.14 1.19 .+-. 0.04 2.18 .+-. 0.30
1.91 .+-. 0.24 19.5 .+-. 11.7 5 2.86 .+-. 0.18 1.19 .+-. 0.05 2.23 .+-. 0.51
1.74 .+-. 0.45 17.9 .+-. 20.3 15 2.81 .+-. 0.14 1.22 .+-. 0.04 2.15 .+-. 0.43
1.90 .+-. 0.38 20.1 .+-. 19.9 35 2.74 .+-. 0.11 1.20 .+-. 0.04 2.62 .+-. 0.21
2.42 .+-. 0.25 2.6 .+-. 7.5 85 2.85 .+-. 0.15 1.20 .+-. 0.06 2.77 .+-. 0.22
2.61 .+-. 0.15 1.6 .+-. 8.1 400 + 2.99 .+-. 0.22 1.12 .+-. 0.06 2.92 .+-.
0.22 2.75 .+-. 0.17 0.32 .+-. 7.1 paryleneN

Detailed Description Paragraph Table - DETL (5):
TABLE 4 One-Month QCA Data (Mean .+-. Standard **Deviation**) Mean Diameter
Mean Diameter Late Paclitaxel Pre-procedure at Follow-up MLD at F/U Loss
(.mu.g) (mm) BAR (mm) (mm) (%) 0 2.80 .+-. 0.14 1.19 .+-. 0.04 2.18 .+-. 0.30
1.91 .+-. 0.24 19.5 .+-. 11.7 5 2.86 .+-. 0.18 1.19 .+-. 0.05 2.23 .+-. 0.51
1.74 .+-. 0.45 17.9 .+-. 20.3 15 2.81 .+-. 0.14 1.22 .+-. 0.04 2.15 .+-. 0.43
1.90 .+-. 0.38 20.1 .+-. 19.9 35 2.74 .+-. 0.11 1.20 .+-. 0.04 2.62 .+-. 0.21
2.42 .+-. 0.25 2.6 .+-. 7.5 85 2.85 .+-. 0.15 1.20 .+-.

0.06 2.77 .+-. 0.22
2.61 .+-. 0.15 1.6 .+-. 8.1 400 + 2.99 .+-. 0.22 1.12
.+-. 0.06 2.92 .+-.
0.22 2.75 .+-. 0.17 0.32 .+-. 7.1 paryleneN

Claims Text - CLTX (6):
3. The device (10) of claim 1 further comprising at least one porous layer (20) posited over the bioactive material layer (18), wherein said at least one porous layer (20) is composed of a **polymer and said polymer** provides for a controlled release of the bioactive material through said at least one porous layer.

Claims Text - CLTX (15):
12. The device (10) of claim 1, wherein the **polymer** is selected from the group consisting of a polyamide, **polymers** of parylene or derivatives thereof, poly(ethylene oxide), poly(ethylene glycol), poly(propylene oxide), silicone based **polymers, polymers** of methane, tetrafluoroethylene or tetramethyidisiloxane or a **polymer** derived from photopolymerizeable monomers.

Claims Text - CLTX (34):
26. The device (10) of claim 25 further comprising at least one porous layer (20) posited over the bioactive material layer (18), wherein said at least one porous layer 20 includes a **polymer and said polymer** provides for a controlled release if the bioactive material thought said at least one porous layer.

Other Reference Publication - OREF (5):
Sushil Sheth, Vishva Dev, Harvey Jacobs, James S. Forrester, Frank Litvack, Neal L. Eigler, Prevention of Subacute Stent Thrombosis by **Polymer**-Polyethylene Oxide-Heparin Coating in the Rabbit Carotid Artery, Feb.

1995, JACC, 1001-29.

Other Reference Publication - OREF (6):
Rajesh K, Aggarwal, Deborah C. Ireland, Michael A. Azrin, Michael D. Ezekowitz, David P. de Bono, Anthony H. Gershlick, "Antithrombotic Potential of **Polymer**-Coated Stents Eluting Platelet Glycoprotein llb/llla Receptor Antibody", Dec., 1996, American Heart Association Circulation, vol. 94, No. 12.